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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,110	08/26/2003	Yanhong Zhu	13131-0292 (44378/287574)	5892

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EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/650,110	ZHU ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-19,21,22 and 24-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-19,21,22 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 17-19, 21-22 and 24-27 are presented for examination.

Applicant's petition for revival after unintentional abandonment filed January 28, 2008 has been received and entered into the present application and was granted March 24, 2008.

Accordingly, prosecution has been reopened.

Applicant's Amendment filed January 28, 2008 has been received and entered into the present application.

Claims 17-19, 21-22 and 24-27 remain pending and under examination. Claims 20, 23 and 28-39 are cancelled and claims 17, 21-22 and 24 are amended.

Applicant's arguments, filed January 28, 2008, have been fully considered. Rejections and objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and objections are either reiterated or newly applied. They constitute the complete set of rejections and objections presently being applied to the instant application.

Objection to the Oath/Declaration

Applicant states that a new oath/declaration will be submitted to overcome the objection raised by the Examiner in the Office Action dated July 24, 2007. However, in view of the fact that a new oath/declaration has not yet been made of record in the instant application, the objection remains proper and is herein repeated below for clarity of the record:

The oath or declaration is defective because Applicant has failed to provide a post office anywhere in the application papers as required by 37 C.F.R. 1.33(a), which was in effect at the time of filing of the oath or declaration. A statement over Applicant's signature providing a complete post office address is required for each of the named inventors. A new oath or declaration in compliance with 37

C.F.R. 1.67(a) identifying this application by serial number and filing date is required. Please reference MPEP §§602.01 and 602.02.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 26 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention, for the reasons of record set forth at page 11 of the previous Office Action dated July 24, 2007, of which said reasons are herein incorporated by reference.

Applicant traverses the instant rejection, stating that the term "increased cholesterol" is a term that was well understood by one of ordinary skill in the art at the time of the invention as evidenced by the publication to Price et al. (copy provided by Applicant; "Observed Changes in the Lipid Profile and Calculated Coronary Risk in Patients Given Dietary Advice in Primary Care", *British Journal of General Practice*, 2000, 50:712-715).

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, the issue at hand is that the term "increased" in the phrase "increased cholesterol" is a relative term. In particular, the term is indefinite because the claims fail to define any standard for ascertaining the requisite amount of cholesterol tolerated by the claims that would be considered "increased". In addition, the specification fails to provide any disclosure of such a standard by which to determine if a patient's cholesterol level is considered "increased" or not commensurate in scope with the claimed subject matter.

The citation to Price et al. not only fails to clarify the term "increased", but also fails to provide a specific standard by which to measure cholesterol levels such that one of ordinary skill in the art at the

time of the invention would have been able to readily identify whether a particular cholesterol level was "increased" or not. In the absence of such a standard by which to compare cholesterol levels to determine if they are "increased" above the normal range, within the normal range or below the normal range, it remains that one of ordinary skill in the art at the time of the invention would not have been reasonably apprised of the standard by which to measure cholesterol levels to determine if such levels meet the instantly claimed limitation of "increased cholesterol levels" as recited in instant claim 26.

For these reasons *supra*, and those previously made of record at page 11 of the Office Action dated July 24, 2007, rejection of claims 26 remains proper and is **maintained**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17-19, 21-22 and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cham (U.S. Patent No. 4,895,558; 1990) in view of Simons et al. ("Cholesterol and Alzheimer's Disease: Is There a Link", *Neurology*, 57; 2001:1089-1093), each already of record, for the reasons of record set

forth at pages 12-14 of the previous Office Action dated July 24, 2007, of which said reasons are herein incorporated by reference.

Cancellation of claims 20, 23 and 39 renders the instant rejection **moot** as applied to such claims.

Newly amended claim 17 remains properly included in the instant rejection because Cham teaches a method for autologous plasma delipidation of animals, including humans (abstract), comprising drawing blood from the animal (i.e., "withdrawing blood containing blood cells from the patient" as in instant claim 17), separating the plasma from the red blood cells (i.e., "separating the blood cells from the blood to yield a naturally occurring plasma from the patient" as in instant claim 17), delipidating the plasma with a lipid solvent [i.e., "exposing the naturally occurring plasma from the patient to a lipid removing agent to derive a partially delipidated plasma having a lower content of at least one of triglycerides or cholesterol than the naturally occurring plasma" as in instant claim 17; note that Cham teaches that the use of a biphasic solvent system for extraction attains complete removal of cholesterol, triglyceride, phospholipid and non-esterified fatty acids of protein denaturation, col.2, l.50-55, and also teaches the use of the butanol-diisopropylether solvent system (an alcohol-ether lipid removing agent as in instant claims 21-22) for partial delipidation of LDL and HDL, col.6, l.3-25], remixing the delipidated plasma with the red blood cells and re-introducing the delipidated blood back into the animal (i.e., "administering to the patient an amount of a composition comprising the partially delipidated plasma" as in instant claim 17; abstract, col.3, l.27-36), such as, e.g., via intravenous infusion (col.3, l.38-41), wherein the delipidation step comprises mixing the plasma with the liquid solvent, allowing the mixture to separate into an organic solvent/lipid phase and an aqueous delipidated plasma phase and drawing off the organic phase (col.3, l.37-42), such as, e.g., via distillation (col.8, l.36-39).

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that Simons et al. fails to teach, suggest or provide motivation to use a plasma delipidation process as disclosed in Cham or as recited in the instant

claims to treat Alzheimer's disease. Applicant further alleges that Cham fails to teach, suggest or provide motivation to use the disclosed autologous plasma delipidation process to treat Alzheimer's disease in a patient. Still further, Applicant asserts that either Simons et al. or Cham, separately or in combination, render the instant claims obvious and alleges that the Examiner has failed to establish a *prima facie* case of obviousness.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

In response to Applicant's argument that the reference to Simons et al. fails to teach or suggest the use of plasma delipidation (such as that disclosed in Cham) and that the reference to Cham fails to teach or suggest the use of the disclosed autologous plasma delipidation process to treat Alzheimer's disease, such remarks are directed toward the individual teachings of each of the cited references without considering the references *as they were combined*. As a result, focusing solely on the discrete teachings of each of the cited references is tantamount to examining each of them inside of a vacuum and fails to be persuasive in establishing non-obviousness because it is the *combined* teachings that are the basis for a proper conclusion of obviousness, not each individual reference alone. In other words, it must be remembered that the references are relied upon in combination and are not meant to be considered separately. To properly conclude obviousness of an invention *does not require the claimed invention to be expressly suggested in its entirety by any one single reference under 35 U.S.C. 103(a)*. Rather, the test is *what the combined teachings* of the references would have suggested to those of ordinary skill in the art. Please reference *In re Young*, 403 F.2d 754, 159 USPQ 725 (CCPA 1968) and *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

In the instant case, clear motivation to combine the cited reference to Cham with that of Simons et al. was provided at pages 13-14 of the previous Office Action dated July 24, 2007, which will not be repeated herein so as not to burden the record but is hereby incorporated by reference. Though it is agreed that neither Cham nor Simons et al. *alone* teaches the entirety of the instantly claimed subject

matter, the fact remains that the cited references, when considered *together*, do, in fact, teach the entirety of the instantly claimed subject matter. Furthermore, a clear statement of motivation to combine the two cited references was provided at pages 13-14 of the previous Office Action as to why one of skill in the art would have been inclined to combine the prior art teachings to Cham and Simons et al. to arrive at the instantly claimed method. In the absence of any specific reasons advanced by Applicant as to why one of skill in the art would not have been motivated to combine Cham and Simons et al., the Examiner defers to the grounds of the rejection as described at pages 12-14 of the previous Office Action to provide the explicit analysis and apparent reason and/or motivation to combine the prior art references in the manner instantly claimed for the reasons described therein.

For these reasons set forth *supra*, and those previously made of record at pages 12-14 of the Office Action dated July 24, 2007, rejection of claims 17-19, 21-22 and 24-27 remains proper and is **maintained**.

Double Patenting

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17-19, 21-22 and 24-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 4,895,558; claims 1-12 of U.S. Patent No. 5,744,038; claims 1-48 of U.S. RE37,584; or claims 1-8, 19-33 and 41-47 of U.S.

RE39,498, each alternatively in view of Simons et al. ("Cholesterol and Alzheimer's Disease: Is There a Link?", *Neurology*, 57; 2001:1089-1093), each already of record, for the reasons of record set forth at pages 14-16 of the previous Office Action dated July 24, 2007, of which said reasons are herein incorporated by reference.

Cancellation of claims 20, 23 and 39 renders the instant rejection **moot** as applied to such claims.

Newly amended claim 17 remains properly included in the present rejection(s) because the claims of each of the cited patents clearly provide for methods of delipidating animal plasma, i.e., removal of cholesterol, triglycerides, and/or other lipids, via the withdrawal of blood from the subject, separating out the blood cells and mixing the plasma with a solvent, such as, e.g., an ether or an ether and alcohol mixture, and then returning the delipidated plasma fraction back into the animal. Please see, e.g., page 15 of the previous Office Action dated July 24, 2007.

Applicant traverses the instant rejections, stating that the patent claims cited by the Examiner are directed to methods of removing cholesterol, triglycerides or lipids from blood or plasma, or to methods of reducing cholesterol, triglycerides or lipids in blood or plasma. Applicant alleges that none of the cited patent claims teach, suggest or provide motivation to apply the methods they recite for treating Alzheimer's disease in a patient. Additionally, Applicant alleges that Simons et al. fails to teach, suggest or provide motivation to use the methods recited in the patent claims to treat Alzheimer's disease in a patient.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

In response to Applicant's argument that none of the cited patent claims teach or suggest the application of the claimed method for treating Alzheimer's disease or that Simons et al. fails to teach or suggest the use of the patented methods for treating Alzheimer's disease, clear motivation *to combine* the cited patent claims with the cited reference to Simons et al. was provided at pages 14-16 of the previous Office Action dated July 24, 2007. Specifically, though the claims of the cited patents provide for

methods of delipidating animal plasma and not specifically for the treatment of Alzheimer's disease, Simons et al. teaches that depletion of cholesterol levels reduces the ability of amyloid-beta to further form amyloid fibrils and amyloid plaques (abstract), which are characteristic of Alzheimer's disease (col.1, p.1089, para.1) and contribute to neurodegeneration (col.1, p.1089, para.1). In view of such a teaching, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ the plasma delipidation process(es) of the patented claims in a patient suffering from Alzheimer's disease as a means for reducing serum and cellular cholesterol levels to thereby treat the disease. Such a person would have been motivated to do so because the prior art of Simons et al. clearly acknowledges the contribution that elevated cholesterol has in effecting an increase in the production and formation of amyloid-beta deposits. Further, the skilled artisan would have had a reasonable expectation of success in treating the condition because the reduction of amyloid-beta deposits, which contribute to the deleterious neurodegenerative effects of Alzheimer's disease, such as, e.g., senility (i.e., dementia), would have ameliorated, or at least slowed the progression of, the neurodegeneration associated with the condition, absent factual evidence to the contrary.

Though it is agreed that the cited patented claims *alone* fail to teach the use of the claimed delipidation process for treating Alzheimer's disease, Applicant is reminded that the obviousness of the instantly claimed subject matter over each of these cited patents was determined based upon the *combination* of the cited patent claims with the teachings of the prior art to Simons et al. Therefore, focusing solely on the discrete teachings of the cited patented claims or the cited reference is tantamount to examining each inside of a vacuum and fails to be persuasive in establishing non-obviousness of the instantly claimed subject matter over the other cited patents because it is the *combined* teachings of the cited patented claims in view of Simons et al. that are the basis for a proper conclusion of obviousness, not each alone. Accordingly, in the absence of any specific reasons advanced by Applicant as to why one of skill in the art would not have been motivated to combine the cited patented claims with the reference

to Simons et al. to arrive at the instantly claimed subject matter, the Examiner defers to the grounds of the rejection as described at pages 14-16 of the previous Office Action to provide the explicit analysis and apparent reason and/or motivation to combine the cited patented claims with the prior art to Simons et al. in the manner instantly claimed for the reasons described therein.

For these reasons set forth *supra*, and those previously made of record at pages 14-16 of the Office Action dated July 24, 2007, rejection of claims 17-19, 21-22 and 24-27 remains proper and is **maintained**.

Conclusion

Rejection of claims 17-19, 21-22 and 24-27 remains proper and is **maintained**.

No claims of the present application are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

May 28, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614